```
=> d his

     (FILE 'HOME' ENTERED AT 16:06:16 ON 11 OCT 2004)

     FILE 'REGISTRY' ENTERED AT 16:06:24 ON 11 OCT 2004
               E ALLOPREGNANOLONE/CN
L1             2 S E3

     FILE 'CAPLUS' ENTERED AT 16:07:34 ON 11 OCT 2004
               S 516-54-1/REG# OR   516-55-2/REG# OR ALLOPREGNANOLONE OR ALLOT

     FILE 'REGISTRY' ENTERED AT 16:11:40 ON 11 OCT 2004
L2             1 S 516-55-2/RN

     FILE 'CAPLUS' ENTERED AT 16:11:40 ON 11 OCT 2004
L3           914 S L2

     FILE 'REGISTRY' ENTERED AT 16:11:41 ON 11 OCT 2004
L4             1 S 516-54-1/RN

     FILE 'CAPLUS' ENTERED AT 16:11:41 ON 11 OCT 2004
L5           765 S L4
L6          1552 S L5 OR L3 OR ALLOPREGNANOLONE OR ALLOTETRAHYDROPROGESTERONE OR
L7         10425 S (CNS OR (CENTRAL)(W)(NERVOUS) OR BRAIN)(2A)INJUR? OR CEREBRAL
L8            10 S L6 AND L7
L9           475 S L6 AND PROGESTERONE AND METABOLITE#
L10          380 S L9 NOT PY>=2000

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 16:49:45 ON
     11 OCT 2004
L11         2262 S L7(L)(SEISURE OR EPILEP?)
L12            0 S (CNS OR (CENTRAL)(W)(NERVOUS) OR BRAIN)(2A)INJUR?(L)(SEISURE#

     FILE 'MEDLINE' ENTERED AT 16:54:14 ON 11 OCT 2004
L13          583 S L11
L14          376 S L13 NOT PY>=2000
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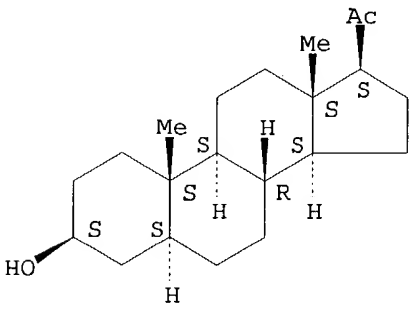
updated search

=> s e3
L1 2 ALLOPREGNANOLONE/CN

=> d rn str cn 1-2

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 516-55-2 REGISTRY

Absolute stereochemistry.

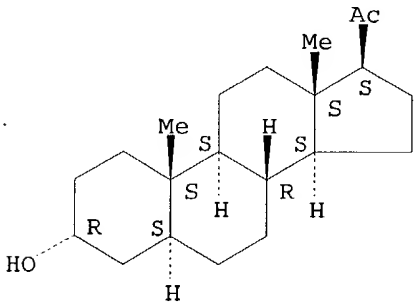


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Pregnan-20-one, 3-hydroxy-, (3β,5α)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5α-Pregnan-20-one, 3β-hydroxy- (6CI, 8CI)
OTHER NAMES:
CN 3-Deoxo-3β-hydroxy-5α-dihydroprogesterone
CN 3β-Allopregnanolone
CN 3β-Hydroxy-5α,17β-pregnan-20-one
CN 3β-Hydroxy-5α-pregnan-20-one
CN 3β-Hydroxy-5α-tetrahydroprogesterone
CN 5α-Dihydropregnenolone
CN 5α-Pregnan-3β-ol-20-one
CN 5α-Pregnane-3β-ol-20-one
CN Allopregnan-3β-ol-20-one
CN **Allopregnanolone**
CN Isopregnanolone
CN NSC 97078
CN U 0949

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 516-54-1 REGISTRY

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Pregnan-20-one, 3-hydroxy-, (3α,5α)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5α-Pregnan-20-one, 3α-hydroxy- (6CI, 8CI)

OTHER NAMES:
CN (+)-3α-Hydroxy-5α-pregnan-20-one
CN (3α)-Allopregnanolone
CN 3α,5α-Pregnanolone
CN 3α,5α-Tetrahydroprogesterone
CN 3α,5α-THP
CN 3α-Hydroxy-5α-dihydroprogesterone
CN 3α-Hydroxy-5α-pregnan-20-one
CN 3α-Hydroxy-5α-pregnane-20-one
CN 5α-Pregnan-3α-ol-20-one
CN 5α-Pregnane-3α-ol-20-one
CN Allopregnan-3α-ol-20-one
CN **Allopregnanolone**
CN Allotetrahydroprogesterone

=> d ibib abs 70,192,352-353,376,276 kwic

L14 ANSWER 70 OF 376 MEDLINE on STN
ACCESSION NUMBER: 97263986 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9109858
TITLE: Seizures, **epilepsy**, and functional recovery after traumatic **brain injury**: a reappraisal.
AUTHOR: Hernandez T D; Naritoku D K
CORPORATE SOURCE: Department of Psychology, University of Colorado, Boulder 80309, USA.
SOURCE: Neurology, (1997 Apr) 48 (4) 803-6. Ref: 47
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970515
TI Seizures, **epilepsy**, and functional recovery after traumatic **brain injury**: a reappraisal.

L14 ANSWER 192 OF 376 MEDLINE on STN
ACCESSION NUMBER: 90184900 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2179001
TITLE: **Epilepsy** in **brain-injured** children.
AUTHOR: Aicardi J
CORPORATE SOURCE: Departement de Pediatrie, Hopital Necker Enfants Malades, Paris, France.
SOURCE: Developmental medicine and child neurology, (1990 Mar) 32 (3) 191-202. Ref: 97
Journal code: 0006761. ISSN: 0012-1622.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900423
TI **Epilepsy** in **brain-injured** children.

L14 ANSWER 352 OF 376 MEDLINE on STN
ACCESSION NUMBER: 60038787 MEDLINE
DOCUMENT NUMBER: PubMed ID: 13719209
TITLE: Clinical and EEG considerations on post-traumatic epilepsy.
AUTHOR: D'ERRICO P
SOURCE: Annali di medicina navale, (1960 Nov-Dec) 65 627-36.
Journal code: 0373072. ISSN: 0392-9418.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: OLDMEDLINE
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990716
Last Updated on STN: 19990716
Entered Medline: 19981101
ST **brain** - wounds and **injuries**; **epilepsy** - etiology

L14 ANSWER 353 OF 376 MEDLINE on STN
ACCESSION NUMBER: 59003191 MEDLINE
DOCUMENT NUMBER: PubMed ID: 13573860

TITLE: Case study of traumatic epilepsy.
AUTHOR: SOUDER C L
SOURCE: Delaware medical journal, (1958 Aug) 30 (8) 223-4.
Journal code: 0370077. ISSN: 0011-7781.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE
OTHER SOURCE: CLML5935-3190-104-201
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000825
Last Updated on STN: 20000825
Entered Medline: 20000701
ST **brain** - wounds and **injuries**; **epilepsy** - etiology and pathogenesis

L14 ANSWER 376 OF 376 MEDLINE on STN
ACCESSION NUMBER: 51000171 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14770621
TITLE: Seizures, head injuries and litigants.
AUTHOR: HYSLOP G H
SOURCE: A. M. A. archives of neurology and psychiatry, (1950 Nov) 64 (5) 736-8.
Journal code: 14470130R. ISSN: 0096-6886.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE
OTHER SOURCE: CLML5120-171-9-138-310-498
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040300
Last Updated on STN: 20040300
Entered Medline: 20040215
ST **brain injury**; **epilepsy**; jurisprudence, medical; malingering

L14 ANSWER 276 OF 376 MEDLINE on STN
ACCESSION NUMBER: 66159235 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4223186
TITLE: [On evaluation of **epilepsy** following closed **brain injury**].
Zur Beurteilung der **Epilepsie** nach gedeckter Hirnverletzung.
AUTHOR: Link K
SOURCE: Monatsschrift fur Unfallheilkunde, Versicherungs-, Versorgungs- und Verkehrsmedizin, (1965 Dec) 68 (12) 539-46.
Journal code: 7505682. ISSN: 0026-9336.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196610
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19661002
TI [On evaluation of **epilepsy** following closed **brain injury**].
Zur Beurteilung der **Epilepsie** nach gedeckter Hirnverletzung.

```
=> s l6 and l7
L8          10 L6 AND L7

=> d ibib abs 1-10

L8   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:776908  CAPLUS
TITLE:                    Progesterone and allopregnanolone reduce
                          inflammatory cytokines after traumatic brain
                          injury
AUTHOR(S):                He, Jun; Evans, Chheng-Orn; Hoffman, Stuart W.;
                          Oyesiku, Nelson M.; Stein, Donald G.
CORPORATE SOURCE:         Department of Psychology, Emory University, Atlanta,
                          GA, 30322, USA
SOURCE:                   Experimental Neurology (2004), 189(2), 404-412
                          CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER:                Elsevier
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Following a traumatic brain injury (TBI), the
     excessive release of interleukin-1β (IL-1β) and tumor necrosis
     factor α (TNF-α) is a major cause of  cerebral
     edema, which, in turn, can cause permanent neuronal loss and
     cognitive deficits in laboratory rats. This study examined the changes in
     expression of the proinflammatory cytokines IL-1β and TNF-α
     after progesterone (8 mg/kg) or allopregnanolone (4 mg/kg)
     treatment in brain-injured rats at 3, 8, and 12 h and
     6 days post-injury. Adult male rats received either bilateral prefrontal
     cortical contusion or sham surgery. The hormones were given i.p. at 1 and
     6 h, and continued once per day for up to 5 days. The gene expression of
     IL-1β and TNF-α was measured by mRNA using real-time quant.
     reverse transcripted polymerase chain reaction (RT-PCR). The protein
     concns. of IL-1β and TNF-α were measured using ELISA (ELISA) to
     confirm the translation from mRNA to protein. The results indicated that
     progesterone and allopregnanolone reduce both IL-1β and
     TNF-α at 3 h post-injury, when the expression of these cytokines
     peaks. At 8 and 12 h post-injury, IL-1β and TNF-α gene
     expression in injured rats was still elevated compared to shams. By the
     sixth day post-injury, cytokine expression was back to the level of intact
     rats. We conclude that progesterone and allopregnanolone may
     attenuate the production of proinflammatory cytokines early after TBI, and
     this may be one mechanism by which progesterone and
     allopregnanolone reduce cerebral edema and
     promote functional recovery from TBI.

L8   ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:370947  CAPLUS
DOCUMENT NUMBER:          140:391399
TITLE:                    Preparation of steroids comprising superoxide
                          dismutase mimic groups and nitric oxide donor groups
                          for therapeutic use in pharmaceutical compositions
INVENTOR(S):              Haj-Yehia, Abdullah Ibrahim
PATENT ASSIGNEE(S):       Yissum Research Development Company of the Hebrew
                          University of Jerusalem, Israel
SOURCE:                   PCT Int. Appl., 138 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2004037843         A2    20040506    WO 2003-IL878            20031024
     WO 2004037843         A3    20040610
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
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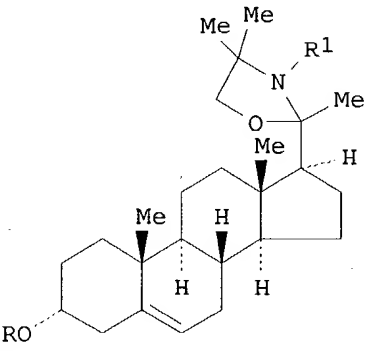
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-421272P P 20021025
OTHER SOURCE(S): MARPAT 140:391399

GI



I

AB This invention relates to methods and devices for administering and to the preparation of multifunctional nitrato-DOXYL-steroids, of the general form R-(ONO2)n [R = steroid containing a heterocyclic nitrogen bonded oxyl radical; n = 1, 2, 3, etc.] combining a steroid component with SOD mimic component and optionally also with a NO donor component, for therapeutic use in treating and preventing disorders associated with oxidative stress and free radical injury, or disorders in which treatment with steroids is indicated, whereas such combination increases the efficacy of treatment and reduces side effects associated with steroid treatment and for treating disorders in which treatment with a smooth muscle relaxant is indicated. The prepared DOXYL-steroids were claimed for use in treating or preventing a disorder selected from the group consisting of respiratory, pulmonary, cardiovascular, inflammatory, and autoimmune disorders. These disorders include asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, chronic obstructive pulmonary diseases (COPD5), bronchial hyperreactivity, respiratory distress syndrome or chronic obstructive airway disease (COAD5), allergic conditions, arthritis, autoimmune hematol. disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-vs.-host disease, multiple sclerosis, Alzheimer's diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, and disorders related to learning. Also, included are disorders related to olfaction, disorders related to nociception, **cerebral edema**, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions, drug and disease-induced neuropathies and nephropathies, pathol. uterine contractions, sinus tachycardia, ischemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders, hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholestemia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion tissue injury, chemotaxis and phagocytic impairment in immunol. disorders, aging-mediated changes, cerebrovascular diseases,

thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection. Thus, nitrato-DOXYL-steroid I (R = NO2, R1 = O.) was prepared via a synthetic sequence which included cyclization of pregnenolone with 2-amino-2-methylpropanol by refluxing 24 h using PTSA to form steroidal oxazolidine I (R = R1 = H) in 92% yield, oxidation of the steroidal oxazolidine with Na2WO4, H2O2 and EDTA at rt for 5 days to give DOXYL-steroidal alc. I (R = H, R1 = O.) in 84% yield, and finally, treatment of the DOXYL-steroidal alc. with N2O4 gas in THF and Et2O at rt for 10-24 h to give the target nitrato-DOXYL-steroid in 98% yield. The DOXYL-steroids were assayed in vitro using a model of biol. response for asthma for relaxation of tracheal rings from guinea pigs.

L8 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:317585 CAPLUS
DOCUMENT NUMBER: 141:65322
TITLE: **Allopregnanolone**, a progesterone metabolite, enhances behavioral recovery and decreases neuronal loss after traumatic **brain injury**
AUTHOR(S): He, Jun; Hoffman, Stuart W.; Stein, Donald G.
CORPORATE SOURCE: Department of Psychology, Emory University, Atlanta, GA, 30322, USA
SOURCE: Restorative Neurology and Neuroscience (2004), 22(1), 19-31
CODEN: RNNEEL; ISSN: 0922-6028
PUBLISHER: IOS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the current study the authors investigated whether **allopregnanolone**, a metabolite of progesterone, could replicate progesterone's beneficial effects in promoting spatial learning ability after bilateral medial prefrontal cortex contusions in rats. **Allopregnanolone** was shown to enhance GABA neurotransmission, whereas its isomer epiallopregnanolone does not have this property. Thus, epiallopregnanolone was chosen as a control substance to examine further the role of GABA transmission in post-trauma neuroprotection. After the contusion, rats were given 4 mg/kg treatment of either **allopregnanolone** or epiallopregnanolone for 5 consecutive days beginning 1h post-injury. Control groups only received vehicle treatment at the same time points. A spatial learning task (Morris Water Maze, MWM) was performed at 7 days post-injury for 10 days. Subsequent histol. analyses of brain tissue were conducted to determine quant. the neuronal losses in both the mediodorsal nucleus of the thalamus (MDN) and the nucleus basalis magnocellularis (NBM). **Allopregnanolone**-treated rats showed better performance in the MWM compared to the vehicle-treated injury group. The histol. analyses also revealed that the **allopregnanolone**-treated injury group had less neuronal loss in both the MDN and the NBM compared to the vehicle-treated injury group. In contrast, epiallopregnanolone did not facilitate MWM performance or reduce neuronal loss in the MDN and the NBM after TBI. Based on these findings, the authors suggest that **allopregnanolone** may mediate the effects of progesterone in promoting cognitive and morphol. recovery from TBI through, among others, its direct or indirect effects on GABA-modulated neurons in the MDN and the NBM.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:212936 CAPLUS
DOCUMENT NUMBER: 141:66617
TITLE: Chronic prenatal ethanol exposure alters hippocampal GABAA receptors and impairs spatial learning in the guinea pig
AUTHOR(S): Iqbal, U.; Dringenberg, H. C.; Brien, J. F.; Reynolds, J. N.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Queen's University, Kingston, ON, K7L 3N6, Can.
SOURCE: Behavioural Brain Research (2004), 150(1-2), 117-125

CODEN: BBREDI; ISSN: 0166-4328
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chronic prenatal ethanol exposure (CPEE) can **injure** the developing **brain**, and may lead to the fetal alc. syndrome (FAS). Previous studies have demonstrated that CPEE upregulates γ-aminobutyric acid type A (GABAA) receptor expression in the cerebral cortex, and decreases functional synaptic plasticity in the hippocampus, in the adult guinea pig. This study tested the hypothesis that CPEE increases GABAA receptor expression in the hippocampus of guinea pig offspring that exhibit cognitive deficits in a hippocampal-dependent spatial learning task. Timed, pregnant guinea pigs were treated with ethanol (4 g/kg maternal body weight per day), isocaloric-sucrose/pair-feeding, or water throughout gestation. GABAA receptor subunit protein expression in the hippocampus was measured at two development ages: near-term fetus and young adult. In young adult guinea pig offspring, CPEE increased spontaneous locomotor activity in the open-field and impaired task acquisition in the Morris water maze. CPEE did not change GABAA receptor subunit protein expression in the near-term fetal hippocampus, but increased expression of the β2/3-subunit of the GABAA receptor in the hippocampus of young adult offspring. CPEE did not change either [3H]flunitrazepam binding or GABA potentiation of [3H]flunitrazepam binding, but decreased the efficacy of **allopregnanolone** potentiation of [3H]flunitrazepam binding, to hippocampal GABAA receptors in adult offspring. Correlational anal. revealed a relationship between increased spontaneous locomotor activity and growth restriction in the hippocampus induced by CPEE. Similarly, an inverse relationship was found between performance in the water maze and the efficacy of **allopregnanolone** potentiation of [3H]flunitrazepam binding in the hippocampus. These data suggest that alterations in hippocampal GABAA receptor expression and pharmacol. properties contribute to hippocampal-related behavioral and cognitive deficits associated with CPEE.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1010568 CAPLUS
DOCUMENT NUMBER: 140:193436
TITLE: **Allopregnanolone** and progesterone decrease cell death and cognitive deficits after a contusion of the rat pre-frontal cortex
AUTHOR(S): Djebaili, M.; Hoffman, S. W.; Stein, D. G.
CORPORATE SOURCE: Cell Biology Building, Department of Emergency Medicine, Brain Research Laboratory, Emory University, Atlanta, GA, 30322, USA
SOURCE: Neuroscience (Oxford, United Kingdom) (2004), 123(2), 349-359
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We compared the effects of three different doses of **allopregnanolone** (4, 8 or 16 mg/kg), a metabolite of progesterone, to progesterone (16 mg/kg) in adult rats with controlled cortical impact to the prefrontal cortex. Injections were given 1 h, 6 h and every day for 5 consecutive days after the injury. One day after injury, both progesterone-treated (16 mg/kg) and **allopregnanolone** (8 or 16 mg/kg)-treated rats showed less caspase-3 activity, and rats treated with **allopregnanolone** (16 mg/kg) showed less DNA fragmentation in the lesion area, indicating reduced apoptosis. Nineteen days after the injury, rats treated with progesterone and **allopregnanolone** (8 or 16 mg/kg) showed no difference in necrotic cavity size but had less cell loss in the medio-dorsal nucleus of the thalamus and less learning and memory impairments compared with the injured vehicle-treated rats. On that same day the injured rats treated with progesterone showed more weight gain compared with the injured rats treated with the vehicle. These

results can be taken to show that progesterone and **allopregnanolone** have similar neuroprotective effects after traumatic **brain injury**, but **allopregnanolone** appears to be more potent than progesterone in facilitating CNS repair.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:821365 CAPLUS
DOCUMENT NUMBER: 140:350664
TITLE: Progesterone in the nervous system: an old player in new roles
AUTHOR(S): Guennoun, R.; De Nicola, A. F.; Schumacher, M.; Baulieu, E. E.
CORPORATE SOURCE: INSERM U488, Bicetre, 94276, Fr.
SOURCE: Hormone Replacement Therapy and the Brain: Current Status of Research and Practice, [based on a Workshop on HRT in Climacteric and Aging Brain], Pisa, Italy, Mar. 15-18, 2003 (2003), 57-71. Editor(s): Gennazzani, Andrea R. Parthenon Publishing Group Ltd.: London, UK.
CODEN: 69ERC8; ISBN: 1-84214-168-6
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review on progesterone, its precursor pregnenolone, and its reduced metabolites 5α-dihydroprogesterone and 3α,5α-tetrahydroprogesterone (**allopregnanolone**) with respect to their biosynthesis and effects in the peripheral and central nervous systems is presented. The review concludes that progesterone, originating either from peripheral glands or synthesized totally in the nervous system, has pos. effects on myelination and neuroprotection. Progesterone effects are pleiotropic and can be achieved via different mechanisms involving different receptors.

REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:650477 CAPLUS
DOCUMENT NUMBER: 140:229650
TITLE: The effects and mechanisms of **allopregnanolone** on promoting behavioral recovery after traumatic **brain injury**
AUTHOR(S): He, Jun
CORPORATE SOURCE: Emory Univ., Atlanta, GA, USA
SOURCE: (2002) 105 pp. Avail.: UMI, Order No. DA3072634 From: Diss. Abstr. Int., B 2003, 63(11), 5563
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:293431 CAPLUS
DOCUMENT NUMBER: 136:304454
TITLE: Methods for the treatment of a traumatic **central nervous** system **injury**
INVENTOR(S): Stein, Donald Gerald; Hoffman, Stuart Wayne
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
---	---	---	---	---

model of epilepsy

AUTHOR(S): Frye, C. A.
CORPORATE SOURCE: Psychology Department, Bates College, Lewiston, ME 04240, USA and Biology Department, Boston University, Boston, MA, 02215, USA

SOURCE: Brain Research (1995), 696(1,2), 113-20
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some anticonvulsant drugs may suppress seizures by enhancing activity of GABAergic systems. Progesterone (P)'s anti-convulsant and neuroprotective effects may be due to the steroid's actions on GABAA-benzodiazepine receptor complexes (GBRs) rather than intracellular progestin receptors (PRs), as many P metabolites have a greater effect in vitro on benzodiazepine binding and Cl- flux than P, but poor affinity for PRs. If P's actions are due to metabolism to a progestin more potent at GBRs, then systemic administration of one of those P metabolites should also prevent CNS damage. To test this hypothesis male rats were implanted with a bipolar electrode, aimed above the perforant pathway. Exptl. animals received the 5α-reduced P metabolite most effective at GBRs, 5α-pregnan-3α-ol-20-one (3α,5α-THP) 2.5 mg/kg s.c., 3 h prior to perforant pathway stimulation, while control animals received sesame oil vehicle. The duration of chewing and drooling, and the incidence of wet dog shakes, partial and full seizures were reduced during perforant pathway stimulation in animals pre-treated with 3α,5α-THP compared to vehicle. Two weeks later, animals pre-treated with 3α,5α-THP had shorter latencies and distances to find a hidden platform in a Morris Water maze task. 3,5-THP pre-treatment also reduced damage to CA1 and CA3 layers of the hippocampus and preserved the number of neurons in the hilar region. These data indicate that the neurosteroid metabolite of P, 3α,5α-THP, can have anticonvulsant and may have neuroprotective effects in an animal model of epilepsy. Further, these data suggest that the mechanism of P's protective and anticonvulsant effects may be via GBRs rather than PRs.